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*STRAIN SPECIFICITY AND PRODUCTION OF ANTIBIOTIC SUBSTANCES. III. PENICILLIUM NOTATUM—CHRYSOGENUM GROUP**

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It has previously been shown[15,20] that although certain groups of microorganisms are characterized by the capacity to produce antibiotic substances, great variation may be found in the quantitative production of the specific substance among the strains within each group. Aside from the natural variation of a group of organisms to bring about a certain physiological reaction, this phenomenon is markedly influenced by three environmental and nutritional factors: (1) the composition of the medium, especially the presence of peptones, carbohydrates and certain growth-promoting or other nutritional substances;[17] (2) conditions of growth, notably aeration and temperature of incubation—some strains grow better in stationary cultures, where they usually produce a surface pellicle, whereas others grow best in submerged and agitated cultures, in the form of suspended colonies or masses of cell material throughout the medium; and (3) changes in the composition of the medium produced by different strains of the same organism—some strains of *Aspergillus clavatus*, for example, change the reaction of the medium to alkaline, rather than to acid, thus favoring the rapid destruction of the antibiotic substance clavacin.[20]

The fact that many microörganisms produce more than one antibiotic substance and the fact that the activity of these substances is measured by a single biological method, based upon their selective antibacterial activity in artificial culture media against a single test organism, often tend to introduce further confusion in the interpretation of the results obtained. The following two illustrations will suffice: (1) The *Penicillium notatum-chrysogenum* group of fungi produce penicillin, a relatively non-toxic compound highly active against gram-positive bacteria, and a protein that functions as a glucose-oxidase and that exerts an antibacterial action only in the

presence of glucose and other carbohydrates. This often tended to confuse the isolation and characterization of penicillin, especially when media used for the testing of the antibiotic substance contained glucose.[8,5,13] (2) The *A. fumigatus* group of fungi produce, in addition to the pigment fumigatin and the non-nitrogenous and sulfur-free fumigacin,[18] also the nitrogen and sulfur-containing gliotoxin.[10,16] The presence[18] or absence[3] of a small amount of gliotoxin admixed with the fumigacin crystals led to its characterization as a different compound.

Another series of complications in the study of antibiotic substances arose from the fact that the same substance may be produced by different fungi. Thus, the designation of a single compound as clavacin, claviformin, patulin and clavatin is based either upon the insufficient characterization of the crude *vs.* the crystalline compounds or upon its production by different types of fungi.[12,7,14]. It is now fairly well established that penicillin or penicillin-like compounds are produced by a large number of different fungi, belonging not only to different species but even to different genera. In spite of this, the substance formed by members of the *A. flavus* group and by different species of *Penicillium* has not only been given different designations (flavicin,[2] flavacidin,[9] gigantic acid[11], parasiticin[4a]) but synonyms have already been piled upon synonyms, with such additional ones as aspergillin and flavatin.

Some of the groups of fungi-producing antibiotic substances show extreme variability in this respect; here belong *A. clavatus* and *A. flavus-oryzae*, discussed previously,[19,15] and *P. notatum-chrysogenum*, the subject of this paper. Different strains obtained from different substrates and, in many instances, isolated from the same mother culture show distinct physiological differences that influence not only the abundance, but often the very nature, of the antibiotic substances produced.[4,6]

Strains Used.—In the following investigations on the production of penicillin and penicillin-like substances by different fungi, 17 cultures were used. These comprised 13 strains of *P. notatum* obtained from different sources, 3 other species of *Penicillium* belonging to the group of green Penicillia, and one species of *Aspergillus*. The numbers and sources of these fungi are briefly summarized:

No. 40. *P. notatum*, received from Dr. C. Thom of Washington, D. C., in 1936, as No. 144-5112.1.

No. 41. *P. notatum*, Fleming strain, received from Dr. C. Thom in December, 1939.

No. 42. *P. notatum*, Westling strain, received from Dr. R. St. John-Brooks of London, in December, 1940, who in turn received it through Dr. H. Raistrick, from C. B. S. Baarn Collection in Holland, in 1925.

No. 43. *P. notatum*, received from Dr. R. St. John-Brooks, in December, 1940, who in turn received it from Dr. Fleming in 1934.

Nos. 44, 45. *P. notatum*, isolated by Prof. A. Callenger of Leeds University, from bread, in 1938, identified by Dr. C. Thom; received from Dr. R. St. John-Brooks in 1940.

No. 46. *P. notatum*, Reid's culture of Fleming's strain, received from Dr. Reid in July, 1941.

No. 47. *P. notatum*, Heatley's culture of Fleming's strain, received from Dr. Heatley in December, 1941.

No. 48. *P. janthinellum*, isolated from the soil and kept for several years in culture collection.

No. 50. *P. notatum*, NRRL No. 832; represents a strain isolated by Dr. Biourge in Belgium, and received from him by C. Thom; received from Dr. K. B. Raper in February, 1943.

No. 51. *P. notatum*, isolated at the NRRL from the Squibb Strain, No. 1249, B21; received from Dr. K. B. Raper in March, 1943.

No. 136. *P. spinulosum*, isolated by Dr. M. B. Morrow of Austin, Texas, from a Guatemala soil; received in August, 1942.

No. 137. *A. flavus*, isolated from the soil in 1941, and found[15] to be capable of producing a penicillin-like substance under certain conditions of culture.

No. 161. *Penicillium* sp. a green Penicillium isolated from the soil in 1941.[17]

No. 7813. *P. notatum;* Dr. C. Thom's culture No. 144B69, received from ATCC, in August, 1943 (NRRL No. 832).

No. 8251. *P. notatum*, Fleming strain, Thom's culture No. 144-5767, received from ATCC, in August, 1943.

No. 8537. *P. notatum* received by the NRRL from Dr. Florey; this is presumably the same culture as No. 47; it was received from the ATCC in August, 1943.

Conditions of Culture.—Three different methods were used for the cultivation of these fungi and for the production of penicillin; namely, the liquid stationary, the liquid submerged, and the deep agar-tube methods. In the first, the medium, consisting of a modified Czapek-Dox broth, with brown sugar in place of glucose, and supplemented with corn steep liquor[15,17] and $CaCO_3$, was placed in Erlenmeyer flasks to a depth of about 1 to 1.5 cm.; the flasks were incubated at about 22°C. for varying periods of time. In the submerged culture, the medium was placed, in 100-ml. portions in 250-ml. flasks, in a shaking machine, and incubated at 28°C. In the third method,[19] a medium similar to the above, but supplemented with 2 per cent agar, was placed in 20-ml. portions in test tubes, measuring 18 × 140 mm., and the tubes were inoculated at the surface.

Methods of Testing.—Three different methods were used for testing the antibiotic activity of the cultures: (1) the dilution method, using the streak agar plate,[21] with *Staphylococcus aureus* or *Bacillus subtilis* as test organism; (2) the agar diffusion or cup method with *B. subtilis* as the test organism;[1] (3) the agar tube method,[19] with *B. subtilis* as the test organism.

Results Obtained.—In the first experiment, the effect of corn steep upon the production of penicillin was determined, using strain No. 50, by growing the culture both in a stationary and a submerged condition. The results (table 1) gave the highest activity for the submerged cultures containing corn steep, a fact already established by workers in the Northern Regional Laboratory. A more detailed study of the production of penicillin under submerged and stationary cultures gave a maximum ac-

tivity in 4 days for the submerged and in 10 to 12 days for the stationary cultures.

A comparison of the production of penicillin by 15 different cultures of fungi, grown under both stationary and submerged conditions (table 2), brought out marked differences in activity. Some of the cultures were found to be highly active under both submerged and stationary conditions (No. 7813); some were inactive or had only limited activity under both conditions (Nos. 41, 43, 44, 45, 48); some gave a higher activity under one set of conditions and others under another. On comparing the course of production of penicillin by *P. notatum* (No. 50) and *A. flavus* (No. 137), both grown in a submerged and agitated state, it was found that although

TABLE 1

PENICILLIN PRODUCTION BY *P. notatum*, AS INFLUENCED BY ADDITION OF CORN STEEP LIQUOR AND BY SHAKING OF CULTURES

MEDIUM	GROWTH OF CULTURES	INCUBATION, DAYS	PLATE METHOD, DILUTION UNITS[a]	CUP METHOD, OXFORD UNITS[b]	pH
BS[c]	Submerged	3	30	0.9	6.7
BS	Submerged	5	100	2.3	8.2
BS	Submerged	7	30	6.3	8.8
BS	Stationary	5	100	0.3	6.0
BS	Stationary	7	<30	1.8	7.2
CSM	Submerged	2	300	5.0	6.5
CSM	Submerged	3	1000	5.4	7.9
CSM	Submerged	5	1000	15.4	8.2
CSM	Submerged	7	300	11.8	8.8
CSM	Stationary	4	<30	1.6	...
CSM	Stationary	5	100	0.5	6.6
CSM	Stationary	7	30	3.7	6.8

[a] *B. subtilis* as test organism.

[b] *Staph. aureus* as test organism.

[c] BS = Brown sugar medium, containing 4 per cent brown sugar and 2 p. p. m. $ZnSO_4.7H_2O$, in addition to other salts; CSM = corn steep medium, containing 2 per cent brown sugar, 1 per cent $CaCO_3$ and 1.5 per cent corn steep, in addition to other salts.

the activity of the first reached a higher maximum, it tended to disappear more rapidly than that of the second. Bacteriostatic spectra of the two culture filtrates were made after 5 days' incubation, when the activity of both was at a maximum, and found to be identical, corresponding to that of isolated penicillin.

The usefulness of the agar tube method for making rapid comparisons of the production of penicillin by different fungi, as well as for studying the effect of the composition of medium and conditions of growth upon this reaction, is illustrated in table 3. When the Czapek-Dox medium was used, No. 136 showed no activity at all; however, in brown-sugar media it proved to be as efficient as two of the best *P. notatum* strains (Nos. 41, 50). On the other hand, No. 161, which was nearly as good as the *P. notatum*

TABLE 2

PRODUCTION OF PENICILLIN BY DIFFERENT STRAINS OF *P. notatum* AND OTHER FUNGI

CULTURE NO.	SUBMERGED CULTURES		STATIONARY CULTURES	
	INCUBATION, DAYS	ACTIVITY, DILUTION UNITS[a]	INCUBATION, DAYS	ACTIVITY, DILUTION UNITS
40	5	50	7	50
40	7	300	..	..
41	7	0	9	0
42	4	20	7	100
42	6	50	9	100
43	7	5	10	..
44	3	0	7	10
44	7	0	..	..
45	4	0	7	10
45	7	0	..	..
46	5	30	9	10
46	7	30	..	..
47	7	50	10	..
47	9	100	..	..
48	5	0	7	0
50	3	150	7	75
50	5	300	..	..
51	7	300	..	..
136	4	300	6	75
136	6	10	..	..
7813	4	1000	7	500
7813	6	1000	9	300
7813	8	1500	..	..
8251	4	30	7	30
8251	6	30	10	30
8537	4	30	7	30
8537	6	100	9	30

[a] *Staph. aureus* used as test organism.

TABLE 3

INFLUENCE OF COMPOSITION OF MEDIUM UPON THE PRODUCTION OF PENICILLIN BY DIFFERENT ORGANISMS, AS MEASURED BY AGAR-TUBE METHOD

5-Day Incubation, Top Layer, Mm. of Zone Produced on *B. subtilis* Inoculated Plate

ORGANISM NO.	COMPOSITION OF MEDIUM			
	CZAPEK-DOX	BROWN SUGAR[a]	CORN STEEP[b]	ZINC[c]
41	19.0	21.0	40.0	41.0
50	19.5	23.0	39.5	39.5
136	0	23.0	36.0	38.0
161	18.0	19.0	26.0	26.0

[a] Brown sugar in place of glucose.

[b] Supplementary to above, 1.5 per cent.

[c] $ZnSO_4 . 7H_2O$, 0.001 per cent, supplementary to above.

strains when grown in the synthetic medium, proved much inferior in the corn steep media.

A comparison of the production and diffusion of penicillin by a larger number of cultures of fungi by the agar tube method is recorded in table 4. Some of the strains that gave rather inferior results in liquid media proved to be excellent producers of penicillin in the agar medium. Number 41, for example, gave virtually no activity in either submerged or stationary cultures, as shown in table 2, but gave excellent activity in the agar culture. Number 46 that gave only low activity in liquid media gave as high activity as the best strain, 7813. These results thus serve to emphasize that the strain of the organism, the conditions of growth and the composition of the medium are the three essential factors in the production of penicillin.

Discussion.—The production of penicillin is not limited to any one species of fungi or even to the genus *Penicillium*. Different species and different

TABLE 4

PENICILLIN PRODUCTION BY DIFFERENT STRAINS OF *P. notatum* AND OTHER FUNGI
Agar-Tube Method, Incubation 6 Days, Mm. of Zone Produced on *B. subtilis* Plate

ORGANISM NO.	TOP OF COLUMN	MIDDLE OF COLUMN	BOTTOM OF COLUMN
40	40.0	32.0	19.5
41	42.5	26.5	0
42	36.3	23.5	0
44	34.8	27.5	0
45	30.8	12.5	0
46	43.0	32.0	16.3
47	40.0	29.8	0
50	43.5	30.5	11.0
136	39.0	31.5	0
161	25.5	11.5	0
7813	44.0	35.8	18.0
8251	39.5	24.5	0
8537	38.5	25.8	0

strains of the same species appear to produce the maximum amount of penicillin or penicillin-like substances under different conditions of culture. Whereas some strains are most active under one set of conditions, other strains exert their greatest activity under other conditions. The fact that, in addition to penicillin, a second antibiotic factor is produced by most of the penicillin-producing fungi further complicates this relationship; this factor may be active only in the presence of glucose, as in the case of the *P. notatum* strains, or its activity may be independent of the glucose in the medium, as in the case of the aspergillic acid produced by *A. flavus*. The production of the second factor is also influenced by the composition of the medium and by conditions of growth.

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[1] Abraham, E. P., Chain, E., Fletcher, C. M., Gardner, A. D., Heatley, N. G.,

Jennings, M. A., and Florey, H. W., *Lancet*, **241**, 177–189; *Nature*, **148**, 758–759; **149**, 356 (1941–1942).

[2] Bush, M. T., and Goth, A., *Jour. Pharmacol.*, **78**, 164–169 (1943).

[3] Chain, E., Florey, H. W., Jennings, M. A., and Williams, T. I., *Brit. Jour. Exp. Path.*, **24**, 108–119; see also Crowfoot, D. M., and Low, B. W., *Ibid.*, **24**, 120 (1943).

[4] Clutterbuck, P. W., Lovell, R., and Raistrick, H., *Biochem. Jour.*, **26**, 1907–1918 (1932).

[4a] Cook, A. H., and Lacey, M. S., *Nature*, **153**, 460 (1944).

[5] Coulthard, C. E., Short, W. F., Skrimshire, G. H. E., Birkinshaw, J. H., Michaelia, R., Sykes, G., Standfast, A. F. B., and Raistrick, H., *Nature*, **150**, 634–645; *Jour. Biol. Chem.*, **148**, 459–460 (1942).

[6] Foster, J. W., Woodruff, H. B., and McDaniel, L. E., *Jour. Bact.*, **46**, 421–433 (1943).

[7] Hooper, I. R., Anderson, H. W., Skell, P., and Carter, H. E., *Science*, **99**, 16 (1944).

[8] Kocholaty, W., *Science*, **97**, 186–187; *Arch. Biochem.*, **2**, 73–86 (1943).

[9] McKee, C. M., Rake, G., and Houck, C. L., *Jour. Bact.*, **47**, 187–197 (1944).

[10] Menzel, A. E. O., Wintersteiner, O., and Hoogerheide, J. C., *Jour. Biol. Chem.*, **152**, 419–429 (1944).

[11] Philpot, F. J., *Nature*, **152**, 725 (1943).

[12] Raistrick, H., Birkinshaw, J. H., Michael, S. E., Bracken, A., Gye, W. E., and Hopkins, W. A., *Lancet*, **245**, 625–635; see also *Ibid.*, **245**, 684 (1943).

[13] Roberts, E. C., Cain, C. K., Muir, R. D., Reithel, F. J., Gaby, W. L., VanBruggen, J. T., Homan, D. M., Katzman, P. A., Jones, L. R., and Doisy, E. A., *Jour. Biol. Chem.*, **147**, 47–58; **148**, 365–378 (1943).

[14] Waksman, S. A., *Science*, **99**, 220–221 (1944).

[15] Waksman, S. A., and Bugie, E., *Proc. Nat. Acad. Sci.*, **29**, 282–288 (1943).

[16] Waksman, S. A., and Geiger, W. B., *Jour. Bact.*, **47**, 391–397 (1944).

[17] Waksman, S. A., and Horning, E., *Mycologia*, **35**, 47–65 (1943).

[18] Waksman, S. A., Horning, E., and Spencer, E. L., *Science*, **96**, 202–203 (1942).

[19] Waksman, S. A., and Reilly, H. C., *Jour. Bact.*, **47**, 308–309 (1944).

[20] Waksman, S. A., and Schatz, A., *Proc. Nat. Acad. Sci.*, **29**, 74–79 (1943).

[21] Waksman, S. A., and Woodruff, H. B., *Jour. Bact.*, **40**, 581–600 (1940).

PERMUTABLE PERIODIC TRANSFORMATIONS

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The so-called "special homologies" were introduced as useful tools[1] in the topology of finite cyclic transformation groups. Up to the present they have found no application in connection with non-cyclic groups. The following remarks indicate, however, that such applications do exist.

Let K be a finite simplicial complex and let $\mathfrak{T} = \{t\}$ be a group of regular[2] simplicial homeomorphisms of K into itself. Let G be an additive

coefficient group. Polynomials in elements of $\mathfrak{T}$ with integer coefficients can be considered as operators on the chains of K, equally well as operators on the homology classes of K since they permute with the boundary operator F. The totality of these operators is a ring $P = \{\rho, \sigma, \ldots\}$ which is commutative when $\mathfrak{T}$ is. We consider only the commutative case in the present note.

We denote by 0 the operator which converts all chains into null chains. Let p be the order of an element t of $\mathfrak{T}$. We denote either one of the operators

$$1 - t, \qquad 1 + t + \ldots + t^{p-1}$$

by $\rho(t)$, the other by $\bar{\rho}(t)$. These elements are zero-divisors of P since $\rho\bar{\rho} = 1 - t^p = 0$.

Given a set of elements $t_1, \ldots, t_m$ of $\mathfrak{T}$, we define a set $I(t_1, \ldots, t_m)$ of simplexes of K by the rule that E is in I if and only if E is invariant under some transformation other than the identity in the subgroup generated by $t_1, \ldots, t_m$.

LEMMA 1. *Let $t_1, \ldots, t_m$ be independent[3] elements of $\mathfrak{T}$ and let X be a chain in $K - I(t_1, \ldots, t_m)$. A necessary and sufficient condition that*

$$\rho(t_1)\rho(t_2) \ldots \rho(t_m)X = 0$$

is that X be expressible in the form

$$X = \bar{\rho}(t_1)Y_1 + \ldots + \bar{\rho}(t_m)Y_m,$$

the Y's being chains in $K - I$.

LEMMA 2. *Let the t's and X be as in lemma 1. A necessary and sufficient condition that*

$$\rho(t_1)X = \ldots = \rho(t_m)X = 0$$

is that X be expressible in the form

$$X = \bar{\rho}(t_1)\bar{\rho}(t_2) \ldots \bar{\rho}(t_m)Z, \qquad Z \subset K - I.$$

A proof of lemma 1 for the case in which $m = 1$ has been given elsewhere[4] and its generalization to arbitrary M is straightforward. Lemma 2 is a fairly direct corollary of lemma 1.

Application. Let p be a prime and let M be a homological n-sphere over the group $\mathfrak{J}_p$ of integers modulo p. Let t be a transformation of period p operating in M. The fixed-point set L of t is[5] a homological r-sphere over $\mathfrak{J}_p$ ($r \leqq n$), possibly null ($r = -1$). If M satisfies certain local conditions, for example if M is locally euclidean, r is necessarily less than n. We assume here that M satisfies such conditions.

THEOREM. *If t and s are permutable transformations of prime period p operating in M and if their fixed-point sets are identical (possibly null), then s is a power of t.*

COROLLARY.[6] *There cannot operate in M a commutative group of fixed-point-free transformations which is of order p^a, $a > 1$, and of type $(p, \ldots, p)$.*

"Fixedpoint-free" refers, of course, to transformations other than the identity.

COROLLARY. *M cannot admit a commutative transformation group of order p^k and type $(p, \ldots, p)$ unless $k \leqq (n+1)/2$.*

We shall prove the theorem for the regular simplicial case and refer elsewhere[7] for the method of passing from the simplicial to the topological case.

We suppose then that M is a finite n-complex and that $I(s) = I(t) = L$, say. L is a homological r-sphere over $\mathfrak{J}_p$. We suppose that s is not a power of t. Then s and t generate a group of order p and type (p, p).

Let $\rho_n, \rho_{n-1}, \ldots$ stand alternately for $1 - t$ and $1 + t + \ldots + t^{p-1}$ and let $\delta = 1 - s$, $\sigma = 1 + s + \ldots + s^{p-1}$. Let $\mathfrak{H}_p^h$ be the group of ρ_h-homology[8] classes of (M, t). There exists for each h a decomposition[9]

$$\mathfrak{H}_p^h = \mathfrak{O}_p^h \times \mathfrak{H}_{0p}^h \tag{1}$$

such that the cycles of $\mathfrak{O}_p^h$ are in $M - L$, those of $\mathfrak{H}_{0p}^h$ in L. Under the present hypotheses *the groups $\mathfrak{O}_p^n, \ldots, \mathfrak{O}_p^{r+1}$ are cyclic[10] of order p* and

$$\mathfrak{H}_p^h = \mathfrak{O}_p^h, \qquad \mathfrak{H}_{0p}^h = 0, \qquad (h = n, \ldots, r+1) \tag{2}$$

$$\mathfrak{H}_p^r = \mathfrak{H}_{0p}^r, \qquad \mathfrak{O}_p^r = 0. \tag{3}$$

We assert that there exist cycles $\Delta^n, \ldots, \Delta^{r+1}$ such that Δ^h is a generator of $\mathfrak{O}_p^h$ and

$$\rho_h \Delta^h = \delta \Delta^h = 0 \qquad (h = n, \ldots, r+1).$$

Let Γ^n be a generator of the ordinary homology group $\mathfrak{H}^n(M, \mathfrak{J}_p)$. Then $s\Gamma^n = k\Gamma^n$, k an integer. Evidently $k^p = 1 \bmod p$ so that $k = 1 \bmod p$. Hence $\delta\Gamma^n = 0$. Similarly $\rho_n \Gamma^n = 0$. This last relation implies that Γ^n is an element, evidently non-zero, of $\mathfrak{H}_p^n$. By (1) we have

$$\Gamma^n = \Delta^n + \Delta_0^n (\Delta^n \subset M - L,\ \Delta_0^n \subset L) \tag{4}$$

where Δ^n, Δ_0^n are elements of $\mathfrak{O}_p^n$, $\mathfrak{H}_{0p}^n$, respectively. Since the latter group is zero, Δ^n cannot be the zero of $\mathfrak{O}_p^n$, hence is a generator. Since all chains in L, in particular Δ_0^n, are annulled[11] by δ and ρ_n, Δ^n is also annulled by δ, ρ_n and therefore has the required properties. Suppose that $\Delta^n, \ldots, \Delta^{h+1}$ $(h > r)$ have been chosen. The relations $\rho_{h+1}\Delta^{h+1} = \delta\Delta^{h+1} = 0$ imply

(lemma 2) $\Delta^{h+1} = \rho_h \sigma Y^{h+1}$ say, where $Y \subset M - L$. Let $\Gamma^h = F(\sigma Y)$. Then

$$\rho_h \Gamma^h = F\rho_h \sigma Y = F\Delta^{h+1} = 0$$
$$\delta \Gamma^h = F\delta\sigma Y = 0.$$

Now Γ^h is precisely the image of Δ^{h+1} under a certain onto-homomorphism[12] $\alpha: \mathfrak{H}_\rho^{h+1} \rightarrow \mathfrak{H}_\rho^h$. Since these groups are both of order p, α is an isomorphism and so Γ^h is a generator of $\mathfrak{H}_\rho^h = \mathfrak{D}_\rho^h$. We then obtain the required Δ^h from Γ^h as for the case $h = n$.

We can now prove the theorem by obtaining the contradiction $\mathfrak{D}_\rho^{r+1} = 0$. As above with h replaced by r, we may write $\Delta^{r+1} = \rho_{r+1}\sigma Y^{r+1}$. Let $\Gamma^{r+1} = F\sigma Y^{r+1}$. As in (4) we have $\Gamma^r = \Delta^r + \Delta_0^r$ ($\Delta_0^r \subset L$) where Δ^r is an element of $\mathfrak{D}_\rho^r$. Since this group vanishes, there exists a special homology

$$F(\rho_r H^{r+1}) = \Delta^r.$$

The boundary of

$$\sigma Y^{r+1} - \rho_r H^{r+1} \tag{5}$$

is $\Delta_0^r \subset L$. This boundary, however, is of the form $\sigma A + \rho_r B$ hence its intersection with L is null.[13] Hence (5) is an absolute cycle and is therefore the boundary of a chain say H^{r+2}. Then

$$F\rho_{r+1}H^{r+2} = \rho_{r+1}\sigma Y^{r+1} - \rho_{r+1}\rho_r H^{r+1}$$
$$= \rho_{r+1}\sigma Y^{r+1} = \Delta^{r+1}$$

so that Δ^{r+1} satisfies a special homology and therefore is the zero of $\mathfrak{D}_\rho^{r+1}$. Since Δ^{r+1} is a generator, we conclude that $\mathfrak{D}_\rho^{r+1} = 0$.

[1] Also called ρ-homologies (5 and 6). All references are to Appendix B of Lefschetz's *Algebraic Topology*.

[2] 1.

[3] The elements $t_1, \ldots, t_m$ are independent if $\Pi t_i^{a_i} = 1$ implies $a_i = 1$ modulo the order of t_i.

[4] 4.1.

[5] (2.1) Theorem.

[6] If $p > 2$, every periodic transformation of an even dimensional euclidean sphere admits fixed points. Hence the corollary is of interest only when n is odd.

[7] 9.

[8] 5 and 6.

[9] 7.1.

[10] 12.

[11] 4.3.

[12] 6 and 10.8.

[13] 4.3.

ON THE ARITHMETIC IN A GROUP RING

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1. Every group $\mathfrak{G}$ of finite order g determines an associative algebra Γ, the group ring, over an arbitrary field K. This algebra consists of all linear combinations

$$\alpha = \sum a_i G_i \tag{1}$$

of the group elements $\mathfrak{G}_i$ with coefficients a_i in K, where equality of these elements, addition and multiplication are defined in the natural manner. The study of the algebra Γ forms one of the most powerful weapons we have for the investigation of groups of finite order. When the field K is of characteristic 0, the algebra Γ is semisimple, and the general principles of the theory of algebras can be applied. As is well known, the ordinary theory of group representations and group characters can be obtained in this way. We then assume that the field K is algebraically closed, or at least that K has the property that all irreducible representations of $\mathfrak{G}$ in K are absolutely irreducible. If the latter condition does not hold in the original field K, it will be satisfied in algebraic extension fields of K of finite degree. Without loss of generality, we may restrict ourselves to the case that K is a suitable algebraic number field,[2] as we shall assume throughout this note.

There can be little doubt that we are far from knowing all important properties of group characters. In particular, we are interested in further results which connect the group characters directly with properties of the abstract group $\mathfrak{G}$. Any result of this kind means, in the last analysis, a result concerning the structure of the general group of finite order.

2. One approach to our question is to study the arithmetic properties of Γ after we study the algebraic properties of Γ. An element α of Γ is said to be an integer, if all the coefficients a_i in (1) are integers of K. The ring J of these integers is not a maximal order,[3] and therefore the ordinary theory of ideals does not hold. However, our definition of integer is linked with the group $\mathfrak{G}$ in a natural manner, and we would lose this connection, if we replaced J by a maximal order. Actually, a study of most arithmetic properties of a maximal order would not lead us beyond the algebraic properties of Γ.

The arithmetic question in which we are mainly interested[4] is the question how a prime ideal $\mathfrak{p}$ of K (or rather its extension $(\mathfrak{p}) = \mathfrak{p}J$ to J) behaves in J. This leads to the study of the residue class ring $J^* = J/(\mathfrak{p})$. But J^* can be interpreted as the group ring of $\mathfrak{G}$ over the field K* of residue

classes of integers of K modulo $\mathfrak{p}$. We thus come back to a study of a group ring and of representations of $\mathfrak{G}$, but now with regard to a modular field K^*. The investigation of $(\mathfrak{p})$ becomes equivalent to the study of the modular representations[5] of $\mathfrak{G}$. For every prime ideal divisor $\mathfrak{P}$ of $(\mathfrak{p})$, the residue class ring $J/\mathfrak{P}$ is a complete matric algebra of a certain degree f over K^*. Thus, $\mathfrak{P}$ defines a modular irreducible representation $\mathfrak{F}$ of $\mathfrak{G}$ of degree f, and we have a (1–1)-correspondence between the prime ideal divisors $\mathfrak{P}_1, \mathfrak{P}_2, \ldots, \mathfrak{P}_k$ of $(\mathfrak{p})$, and the irreducible modular representations $\mathfrak{F}_1, \mathfrak{F}_2, \ldots, \mathfrak{F}_k$ of $\mathfrak{G}$.

Since J is not a maximal order, we cannot write $(\mathfrak{p})$ as a product of powers of the $\mathfrak{P}_i$. However, we still have a unique representation of $(\mathfrak{p})$ as a direct intersection of ideals

$$(\mathfrak{p}) = \mathfrak{M}_1 \cap \mathfrak{M}_2 \cap \ldots \cap \mathfrak{M}_t. \tag{2}$$

Here, any two of the $\mathfrak{M}_\tau$ are relatively prime, and no $\mathfrak{M}_\tau$ can be written as an intersection of relatively prime ideals which are different from $\mathfrak{M}_\tau$. The $\mathfrak{P}_i$ dividing a fixed $\mathfrak{M}_\tau$ form a "block" B_τ, and according to what we said above, we may also speak of the modular representations $\mathfrak{F}_i$ belonging to the block B_τ. Every $\mathfrak{F}_i$ then belongs to exactly one block. Finally, we may associate every ordinary irreducible representation $\mathfrak{Z}_j$ of $\mathfrak{G}$ with exactly one block B_τ.[6] Every $\mathfrak{Z}_j$ of the block B_τ contains only modular constituents $\mathfrak{F}_i$ of B_τ, and, conversely, every $\mathfrak{F}_i$ of B_τ appears only in $\mathfrak{Z}_j$ of B_τ. This shows that there exists a connection between the decomposition (2) and the decomposition of Γ into a direct sum of simple algebras.

Denote by p the rational prime number which is divisible by $\mathfrak{p}$. If p^α is the highest power of p which divides all degrees f_i of the $\mathfrak{F}_i$ belonging to the block B_τ, then p^α also is the highest power of p which divides the degrees z_j of all ordinary representations $\mathfrak{Z}_j$ of B_τ.[7] We then say that the block B_τ is of *type* α. If p^a is the highest power of p dividing the order g of $\mathfrak{G}$, then we call $d = a - \alpha$ the *defect* of B_τ. The smaller d, the simpler is the structure of $\mathfrak{M}_\tau$ in (2).

If the group characters of $\mathfrak{G}$ are known, we can easily obtain the blocks $B_1, B_2, \ldots, B_t$. The main object of this paper is to give a direct characterization of the blocks. For instance, we shall show that the number of blocks of given positive defect d is completely determined by the structure of certain subgroups $\mathfrak{N}$ of $\mathfrak{G}$ which are the normalizers $\mathfrak{N}$ of the subgroups $\mathfrak{H}$ of order p^d in $\mathfrak{G}$.

3. The modular group ring $J/(\mathfrak{p})$ determines a matrix C of Cartan invariants.[8] This C is the direct sum of the matrices C_τ of Cartan invariants of the rings $J/\mathfrak{M}_\tau$ corresponding to the blocks B_τ. The degree of C_τ is equal to the number y_τ of prime ideals $\mathfrak{P}_i$ (and of modular representations $\mathfrak{F}_i$) in the block. The matrix C_τ is symmetric, the corresponding

quadratic form is non-negative, the determinant of C_τ is a power of p. The coefficients c_{ij} are non-negative rational integers, the value of c_{ij} depends on the mutual relation of the prime ideals $\mathfrak{P}_i$ and $\mathfrak{P}_j$.

It is easy to determine the elementary divisors of C. Let $K_1, K_2, \ldots, K_k$ be the classes of conjugate elements of $\mathfrak{G}$ which contain *p-regular elements*, i.e., elements whose order is prime to p. Let g_λ be the number of elements in K_λ so that $g_\lambda = g/n_\lambda$ where n_λ is the order of the normalizer of the elements of K_λ, and suppose that p divides n_λ exactly with the exponent ρ_λ. Then $p^{\rho_1}, p^{\rho_2}, \ldots, p^{\rho_k}$ are the elementary divisors of C.[9] Exactly y_τ of these elementary divisors must belong to C_τ, and naturally the question arises in what manner the k elementary divisors of C are distributed into blocks. A partial answer is given by

THEOREM 1: *If C_τ is the Cartan matrix of a block of defect d, then C_τ has one elementary divisor p^d while all other elementary divisors of C_τ are powers of p with exponents smaller than d.*

As corollaries[10] we obtain

COROLLARY 1: *If there exist l_σ p-regular classes K_λ in $\mathfrak{G}$ for which the order of the normalizer of the elements is divisible by p^σ but not by $p^{\sigma+1}$, then $\mathfrak{G}$ possesses at most l_σ blocks of defect σ ($\sigma = 0, 1, 2, \ldots, a$).*

COROLLARY 2: *There exist exactly l_a blocks of maximal defect a, where $g \equiv 0 \pmod{p^a}$, $g \not\equiv 0 \pmod{p^{a+1}}$.*

COROLLARY 3: *If B_τ is a block of defect 0, then C_τ has the degree 1, and its only coefficient is 1. The block consists of exactly one ordinary representation $\mathfrak{Z}$ and one modular representation $\mathfrak{F}$. Taken as a modular representation, $\mathfrak{Z}$ remains irreducible and coincides with $\mathfrak{F}$. The prime ideal $\mathfrak{P}$ belonging to $\mathfrak{F}$ coincides with $\mathfrak{M}_\tau$ in (2).*

In the proof of theorem 1, the following construction can be used. Consider the k columns of the matrix of group characters of $\mathfrak{G}$ which belong to the p-regular classes $K_1, K_2, \ldots, K_k$ of $\mathfrak{G}$. It is possible to select a minor of degree k which is not divisible by $\mathfrak{p}$. Exactly y_τ of the rows in this minor must belong to ordinary characters ζ_μ of B_τ. It is then possible to associate y_τ of the columns with B_τ, such that each column belongs to exactly one B_τ, and that the y_τ rows and columns associated with B_τ form a minor which is not divisible by $\mathfrak{p}$. (This construction may not be unique.) We can then prove

THEOREM 2: *If the classes $K_\lambda, K_\mu, K_\nu, \ldots$ are associated with the block B_τ by the preceding construction, and if p divides the order of the normalizers of the elements of K_i to the exact exponent ρ_i, then the elementary divisors of C_τ are the powers of p with the exponents $\rho_\lambda, \rho_\mu, \rho_\nu, \ldots$.*

If ζ_μ is an ordinary character of $\mathfrak{G}$, and if $\zeta_\mu(K_\nu)$ is the value of ζ_μ for the elements of K_ν, then it is well known that the numbers

$$\omega_\mu(K_\nu) = g_\nu \zeta_\mu(K_\nu)/Dg(\zeta_\mu) \qquad (3)$$

are algebraic integers. The proof of theorems 1 and 2 yields at the same time

THEOREM 3: *A character ζ_μ belongs to a block B_τ of a defect larger than or equal to a given number d, if and only if we have $\omega_\mu(K_\nu) \equiv 0 \pmod{\mathfrak{p}}$ for all p-regular classes with $\rho_\nu < d$. Two characters ζ_λ and ζ_μ belonging to blocks of defect d appear in the same block, if and only if*

$$\omega_\lambda(K_\nu) \equiv \omega_\mu(K_\nu) \pmod{\mathfrak{p}}$$

for all p-regular classes with $\rho_\nu = d$.

COROLLARY 4: *If the Cartan matrix C_τ of the block B_τ of defect d has h elementary divisors p^{d-1}, then B_τ contains at least $h + 1$ ordinary characters whose degrees are not divisible by p^{a-d+1}.* (By definition, the degrees are all divisible by p^{a-d}.)

4. If K_α is a class of conjugate elements of $\mathfrak{G}$, we also denote by K_α the sum of all the elements in this class. As is well known, the K_α then form a basis of the center Λ of the group ring Γ. We thus have formulae

$$K_\alpha K_\beta = \sum a_{\alpha\beta\gamma} K_\gamma \quad . \qquad (4)$$

where the $a_{\alpha\beta\gamma}$ are non-negative rational integers. The true significance of the numbers ω_μ in (3) is that they form a character of the commutative algebra Λ. Taking the $\omega_\mu \pmod{\mathfrak{p}}$, we obtain a modular character of Λ, or what is the same thing, a character of the center Λ^* of the modular group ring Γ^*. But characters ζ_μ of $\mathfrak{G}$ belonging to the same block B_τ give rise to the same modular character of Λ. Hence we have a (1–1) correspondence between the blocks B_τ of $\mathfrak{G}$ and the characters of the commutative modular algebra Λ^*.

It is easy to prove certain arithmetic properties of the $a_{\alpha\beta\gamma}$ in (4). For instance, if an element G of K_γ commutes with all elements of a subgroup $\mathfrak{H}$ of order p^d of $\mathfrak{G}$ while no element of K_α commutes with all elements of $\mathfrak{H}$, then $a_{\alpha\beta\gamma}$ must be divisible by p. On the basis of this remark and more general statements of a similar nature, it is possible to establish connections between $\Lambda^* = \Lambda^*(\mathfrak{G})$ and the analogous algebras $\Lambda^*(\mathfrak{N})$, formed by means of suitable subgroups $\mathfrak{N}$ of $\mathfrak{G}$. In this manner we obtain a connection between the characters of $\Lambda^*(\mathfrak{G})$ and those of $\Lambda^*(\mathfrak{N})$, and finally a connection between the blocks of $\mathfrak{G}$ and certain blocks of $\mathfrak{N}$. Our main results are proved by combining this method with that of section 3. They are contained in the following theorems:

THEOREM 4: *Choose one group $\mathfrak{H}_\sigma$ of order p^d from each class of conjugate subgroups of this order of $\mathfrak{G}$, and denote the normalizer of $\mathfrak{H}_\sigma$ by $\mathfrak{N}_\sigma$ ($\sigma = 1, 2, \ldots, l$). For the given prime p, all blocks of $\mathfrak{N}_\sigma$ have at least the defect d. If $\mathfrak{N}_\sigma$ possesses exactly r_σ blocks of defect d, then $\mathfrak{G}$ contains exactly $r_1 + r_2 + \ldots + r_l$ blocks of defect d.*

THEOREM 5: *To every block B of defect d of $\mathfrak{G}$ there corresponds uniquely a block $\tilde{B}$ of defect d of one of the $\mathfrak{N}_\sigma$ in theorem 4. If $\omega_\mu(K_\nu)$ in (3) is formed by means of a character of B while $\tilde{\omega}_\lambda(\tilde{K}_\iota)$ is formed in an analogous manner by means of a character of $\tilde{B}$, then*

$$\omega_\mu(K_\alpha) \equiv \sum_\beta \tilde{\omega}_\nu(\tilde{K}_\beta) \pmod{\mathfrak{p}}. \tag{5}$$

Here, K_α is any class of $\mathfrak{G}$, while $\tilde{K}_\beta$ ranges over all classes of $\mathfrak{N}_\sigma$ which lie in K_α and whose elements belong to the centralizer $\mathfrak{T}_\sigma$ of $\mathfrak{H}_\sigma$. The ideal $\mathfrak{p}$ denotes a fixed prime ideal divisor of p in the field generated by the characters of B and $\tilde{B}$.

COROLLARY 5: *If in the notation of theorem 5, the class K_α does not contain elements of $\mathfrak{T}_\sigma$ then*

$$\omega_\mu(K_\alpha) \equiv 0 \pmod{\mathfrak{p}} \tag{6}$$

If K_α contains elements of $\mathfrak{T}_\sigma$, and if the order of the normalizer of these elements is not divisible by p^{d+1}, then K_α contains only one class $\tilde{K}_\beta$ which consists of elements of $\mathfrak{T}_\sigma$, and we have

$$\omega_\mu(K_\alpha) \equiv \tilde{\omega}_\nu(\tilde{K}_\beta) \pmod{\mathfrak{p}}. \tag{7}$$

The congruences (5), (6) and (7) can be expressed in terms of the characters. We thus obtain the following relations between the characters of $\mathfrak{G}$ and those of $\mathfrak{N}_\sigma$.

COROLLARY 6: *Let ζ_μ by any character of B, say of degree z, let $\tilde{\zeta}_\nu$ be a character of the corresponding block $\tilde{B}$ of $\mathfrak{N}_\sigma$, say of degree w. In the notation of theorem 5, we have*

$$\zeta_\mu(K_\alpha) \equiv \frac{z}{w g_\alpha} \sum_\beta \tilde{g}_\beta \tilde{\zeta}_\nu(\tilde{K}_\beta) \pmod{\mathfrak{p}p^m} \quad \text{with } m = s - a + \rho_\alpha$$

where g_α is the number of elements in K_α, $\tilde{g}_\beta$ is the number of elements in $\tilde{K}_\beta$, ρ_α is the exponent to which p divides $n_\alpha = g/g_\alpha$, and s is the exponent to which p divides z. In the case of (6), this yields

$$\zeta_\mu(K_\alpha) = 0 \pmod{\mathfrak{p}p^m},$$

while in the case of (7) we obtain

$$\zeta_\mu(K_\alpha) \equiv \frac{zn}{wg} \tilde{\zeta}_\nu(\tilde{K}_\beta) \pmod{\mathfrak{p}p^{s-a+d}}$$

where n is the order of $\mathfrak{N}_\sigma$.

Our results do not give any new information about the blocks of highest kind, i.e., of defect 0. We have here $\mathfrak{H} = \{1\}$, $\mathfrak{T}_\sigma = \mathfrak{N}_\sigma = \mathfrak{G}$. For blocks of positive defect d, we may have $\mathfrak{N}_\sigma = \mathfrak{G}$, but only when $\mathfrak{G}$ has a normal subgroup of an order $p^d > 1$. In any case, every block of defect d of $\mathfrak{N}_\sigma$

contains an ordinary representation which associates the unit matrix with the elements of $\mathfrak{H}_\sigma$. As a representation of $\mathfrak{N}_\sigma/\mathfrak{H}_\sigma$ this one is of the highest kind. This shows that the question of finding all blocks of defect $d > 0$ can be answered by studying groups of smaller order than g. If for every one of these B we know the number of ordinary characters contained in B, we also know the number of blocks of defect 0. By corollary 3, it is the number of classes of $\mathfrak{G}$, diminished by the number of ordinary characters which belong to blocks of positive defect.

In finding all blocks of $\mathfrak{G}$, the following remark is useful.

REMARK: In theorems 4 and 5, it is sufficient to consider only groups $\mathfrak{H}_\sigma$ which are p-Sylow-subgroups of normalizers of p-regular elements, and for which $\mathfrak{H}_\sigma$ is a maximal normal p-subgroup of $\mathfrak{N}_\sigma$. If these assumptions are not satisfied, $\mathfrak{H}_\sigma$ does not possess blocks of defect d.

[1] The work on this note was done while the author was a Fellow of the John Simon Guggenheim Memorial Foundation.

[2] Using a theorem of Hasse, *Jour. f. d. reine u. angew. Math.*, **167**, 399–404 (1931), we could even assume that K was obtained from the field of rational numbers by the adjunction of a certain root of unity.

[3] For the arithmetic in maximal orders of algebras, see, for instance, Jacobson, N., "The Theory of Rings," Math. Surveys No. II (1943).

[4] For the following cf. Brauer, R., these PROCEEDINGS, **25**, 252–258 (1939).

[5] For the modular representations of groups, cf. Brauer, R., and Nesbitt, C., University of Toronto Studies, Math. Ser. No. 4 (1937), and *Ann. Math.*, **42**, 556–590 (1941). I refer to the second of these papers as BN.

[6] Cf. BN, §9.

[7] BN, §17.

[8] BN, § 5.

[9] BN, § 16.

[10] Corollary 1 is an improvement of theorem 3 of BN. Corollary 2 is identical with theorem 2 of BN. Corollary 3 is identical with theorem 1 of BN.

POSSIBLE NUMBERS OF NON-INVARIANT OPERATORS OF A GROUP

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In a preceding number of these *Proceedings* (**30**, 25–28 (1944)), it was noted that a necessary and sufficient condition that there is a group in which the number of the non-invariant operators is a given prime number p is that there is a group of order $p + 1$ which contains no invariant operator besides the identity. From this theorem it follows that the only odd prime numbers which are less than 100 and are not equal to the number of the

non-invariant operators in some group are 3, 7, 31, 43. It is obvious that there is no group which contains exactly two or four non-invariant operators and if a group contains exactly five non-invariant operators it is the non-cyclic group of order 6. Each of the two non-abelian groups of order 8 contains exactly six non-invariant operators and these are the only groups which have this property.

From the noted theorem it results that whenever a prime number is of the form $2^n - 1$ it cannot represent the number of the non-invariant operators of any group. In particular, there is no group which contains exactly seven non-invariant operators. There is also no group which contains exactly eight non-invariant operators since the smallest number of non-invariant operators in a non-abelian group of order g is known to be $3g/4$ and the non-abelian group of order 10 contains nine non-invariant operators. The tetrahedral group is known to contain eleven non-invariant operators while each of the other two non-abelian groups of order 12 clearly contains exactly ten non-invariant operators. We have now noted all the possible non-abelian groups which separately contain no more than eleven non-invariant operators.

Suppose that the order of the central quotient group of a given group G is a power of a prime number. A Sylow subgroup of G whose order is a power of this prime number contains an invariant subgroup whose order is this prime number. The operators of this invariant subgroup are commutative with every operator in the central of G and also with at least one operator of G corresponding to every operator in the central quotient group G. Hence these operators appear in the central of G, which is contrary to the hypothesis unless the central is divisible by the prime number which divides the order of this central quotient group. Hence we have proved the following theorem: *When the order of the central quotient group of G is a certain power of a prime number then the order of G is divisible by a higher power of this prime number and hence the order of the central of G is divisible by this prime number.*

If a given group G contains exactly n non-invariant operators then the direct product of G and an arbitrary abelian group contains exactly n times the order of this abelian group invariant operators. In particular, from the fact that there is a group which contains exactly five non-invariant operators it results directly that there is at least one group which contains an arbitrary multiple of five non-invariant operators. We have seen that there are two and only two groups which separately contain ten non-invariant operators but it is obvious that there is only one group which contains exactly fifteen non-invariant operators since *a group whose central involves one of its Sylow subgroups and whose order is divisible by only two distinct prime numbers is the direct product of its Sylow subgroups.* In particular, the central of a group of order 20 cannot be of order 5.

It was noted above that both the dihedral group of order 6 and the dihedral group of order 10 are completely determined by the number of their respective non-invariant operators. To construct a system of groups which has the property that every group contained in the system is completely determined by the number of the non-invariant operators contained in the group we may note that whenever $2p - 1$ is a prime number, where p is also a prime number, the dihedral group of order $2p$ contains a prime number of non-invariant operators. Since there is one and only one dihedral group of order $2p$ and this contains no invariant operator besides the identity when p is odd it results that each of these groups is completely determined by the number of its non-invariant operators. The three lowest orders of such groups are 6, 14, 38.

Although there are many groups which are completely determined by the number of their non-invariant operators and this number therefore serves as a complete definition of these groups there are also many cases in which different groups have the same number of non-invariant operators. It was noted above that the two non-abelian groups of order 8 and two of the three non-abelian groups of order 12 have this property. Among the nine non-abelian groups of order 16 there are six which have a central of order 4 and hence they contain exactly twelve non-invariant operators. The three remaining non-abelian groups of order 16 contain a central of order 2 and hence involve separately fourteen non-invariant operators in each case. Since the groups of order 16 have been widely published it may be assumed that these cases are known. They represent the only groups which contain exactly either twelve or fourteen non-invariant operators.

We have now incidentally noted that each of the natural numbers which are less than 16 except 1, 2, 3, 4, 7, 8 is equal to the number of the non-invariant operators in at least one group. To prove that there is no group which has exactly sixteen non-invariant operators we may first note that the order of such a group could not be 18 for it would then contain a central of order 2 and hence it would contain only one subgroup of this order and this would be a Sylow subgroup. For similar reasons it could not be of order 20. It could not be of a larger order since at least three-fourths of the operators of every non-abelian group are non-invariant. There exists therefore no group which contains exactly sixteen non-invariant operators. In fact, there exists no group which has exactly a power of 2 less than 2^7 non-invariant operators.

If a group contains exactly seventeen non-invariant operators it is either the dihedral or the generalized dihedral group of order 18 and if it contains exactly eighteen non-invariant operators its order could not exceed 24. If it is of order 24 its central must contain its Sylow subgroup of order 3 and hence it must be the direct product of a group of order 3 and one of the two non-abelian groups of order 8 according to the theorem noted above.

If it is of order 20 it is either the dihedral or the dicyclic group of this order and hence there are exactly four groups which have the property that each of them contains exactly eighteen non-invariant operators. Since a group which involves exactly nineteen non-invariant operators is the metacyclic group of order 20 it is completely determined by the number of its non-invariant operators and the two noted groups of order 18 are the only groups up to order 20 which contain exactly a prime number of non-invariant operators but are not completely determined by this number.

The alternating group G of order 60 is known to be the group of smallest composite order which is simple. We proceed to prove that this group is completely determined by the fact that it contains exactly fifty-nine non-invariant operators. To prove this fact it may first be noted that since fifty-nine is a prime number the number of the groups which contain exactly fifty-nine non-invariant operators is equal to the number of groups of order 60 which separately have the property that each of them contains no invariant operator besides the identity. If a group of order 60 contains no invariant operator besides the identity it involves six subgroups of order 5 which it transforms according to a transitive group of degree 6. This transitive permutation group must be of order 60 since each of its six subgroups of order 5 transforms the remaining five subgroups of this order contained in G among themselves but not invariantly.

Hence, the permutation group according to which G transforms its six subgroups of order 5 is simply isomorphic with G and there is therefore only one permutation group of degree six and of order 60 which is simply isomorphic with G, and hence the simple group of order 60 is completely determined by the fact that it contains fifty-nine non-invariant operators. The fact that the alternating group of degree five is the simple group of smallest composite order was noted already by E. Galois (1811–1832). The fact that this group is completely determined by the number of its non-invariant operators furnishes a new definition of this important simple group of composite order. Various other definitions of this group are known.

THE BIOLOGICAL EFFECTS OF X-RAYS AS A FUNCTION OF INTENSITY

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The factors which are influencing the biological action of radiations naturally received a great deal of attention. The prevailing opinion seems to be that the biological effects of radiations are a function only of the energy of the absorbed rays. This view seems to be reasonably well established for radiations of x-ray frequency.[1] In the range of frequencies of the band of ultra-violet radiations the effect seems to depend on the particular wave length.[2]

The effects of other radiations, such as neutrons or alpha particles appears to be also a function of the total energy absorbed, though in this case the energy of the individual particles seems to be a factor as well.[3] However, the effects of a given amount of energy of neutron rays are different from the effects produced by the same amount of absorbed x-ray energy. The ratio of effectiveness of a given amount of neutron ray energy is many times as great as the absorption of the same amount of x-ray energy. This ratio does not at all remain constant but varies for different effects and with different specimens. In the case of mutation of drosophila the ratio is 2:1; for the effects on carcinoma, is 6:1; for the recessive effects on wheat the ratio is 20:1 and so on.[4]

The difference in the action of the two types of radiation is, in the opinion of Zircle[3] and of Failla,[1] due to the greater intensity of radiation produced by neutron and alpha rays compared with the intensity of ionization produced by x-rays. Zircle points out that the ratio of the intensities of the two types of radiation is of the order of 100:1. In very careful experiments Zircle showed that the biological effects of alpha particles vary approximately with the 2.5 power of that intensity.

The view that the intensity of ionization is responsible for the difference in the biological action of the various radiations seems to have a great deal in its favor. The seat of the action of x-rays or of other types of radiations are the cells or some parts of the cell. The exchange of nutrients of this part of the cell with the rest of the organism must depend upon the boundary of the affected region. The ability to exchange products with the neighboring regions is profoundly affected by the electrical conditions in that boundary. It seems, therefore, reasonable to assume that high ionization near the boundary of a given region may profoundly affect the biological action of that region.

In the case of x-rays no intensity effects have been observed so far as the author is aware. It is possible that the x-ray energy was in all cases

administered at such low intensities that the effects escaped the attention of the workers.

It seemed worth while to investigate whether the biological effects of a given dose of x-rays administered at a very high intensity are different from the effects produced by an equal dose at moderate intensities.

The source of x-rays was a deep therapy tungsten target water cooled Coolidge x-ray tube with a 45 degree focus. The tube was run at about 70,000 volts and 10 milliamperes. For most measurements the radiation was filtered with 1.2 mms. of aluminum. All these factors were kept constant in order to have the same band of radiations. The only factor that was varied was the distance from the tube. The construction of the tube was such that specimens could be placed at a distance of 6 cms. from the target. The distance was varied from 60 cms. to 6 cms. with a variation of the intensity of radiation from 25 to 2500 r/min. No experiments were made at longer distances from the target.

In order to increase the range of intensities, experiments were also conducted with unfiltered radiation at the smallest distance from the target, namely 6 cms. Since the quality of the unfiltered radiation was different from the filtered it seemed advisable to determine the relative effectiveness of the two types at low intensities in order that the intensity effect, if present, should not mask the comparison. The effect on seeds of wheat of unfiltered and filtered radiation were observed at a distance of 60 cms. from the target. The radiation at this distance was, doubtless, too weak to have an intensity effect. It was found that the time necessary to produce a given effect (per cent growth) with unfiltered rays was approximately one-half that of the filtered. The intensity of the unfiltered radiation at a distance of 6 cms. from the target was thus about 5000 r/min. The experiments were run for eight different intensities of radiation ranging from 25 r/min. to 5000 r/min.

The choice of a suitable biological material proved to be most difficult. Many unsuccessful experiments have been made with beans, peas and corn. Unfortunately the variation between individual species was much too great. Also, the variation of the effects of a given dose of x-rays even when the seeds were inbred was so great as to render the results doubtful, except for a prohibitively large number of measurements. The seeds of wheat proved to be more free from these defects than any other material tried and were finally adopted for the purpose. The Big Club variety was selected chiefly because some work has already been done on these seeds.

The experiments extended for a period of over two years. While the results obtained during the first year were quite consistent, the wheat seedlings were very defective that year, and it seemed advisable to repeat the experiment with a new and more vigorous crop. This was done last fall. The procedure followed was that employed by Zircle and Aebersold.[4]

The seeds were allowed to soak in water for 3 hours. They were then spread in trays over moist filter paper. After about 12 hours the seeds were placed on small plates, 30 seeds on each plate, and exposed to x-rays. After 48 hours of sprouting, the length of the stems was measured, and this length was used as the biological indicator. During Winter the variation in the temperature of the rooms was too great to follow this procedure. In some cases the rooms were so cold that even after 48 hours the growth was very small; on the other hand the growth was excessive at other times when the rooms were over-heated. Instead of following the practice of measuring the length of the seeds 48 hours after exposure to x-rays, the procedure was adopted of examining the seeds only after the average of the controls reached a height of about 45 mms. Later experiments were conducted with

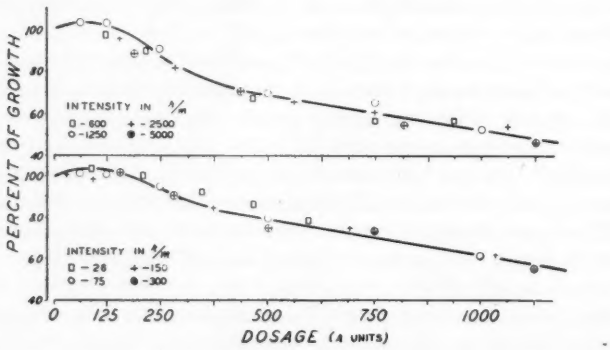

FIGURE 1

the seeds in a constant temperature enclosure. This method gave the best results so far as the magnitude of the spread from the mean is concerned.

The variation of the length of the stem was used as the criterion of the effects of radiation, and no attention was paid to the roots. The reason for neglecting these data was the great variability of the root system. In some plants the roots were short and stubby, while in others they were long and slender. Also the number differed with different plants—some had two, while others had three or four.

The variation of the length of the stem as a function of the dose was studied at various intensities of x-rays. Data were also taken for a given dose at intensities varying from the smallest to the largest. Figure 1 shows the variation of the per cent of growth as a function of the dose with radiations at various intensities. It was subdivided into two curves in order to show more conveniently the results of the measurements with the eight different intensities. Each point represents the average of about 200 meas-

urements. It is evident that the various intensities do not produce any marked differences in the results.

In figure 2 are shown the variations of the per cent growth for a given dose with the intensity of radiation. In these curves are incorporated data obtained in figure 1 and also data of experiments which were run especially for this purpose. Again it is evident that no significant variations with intensity are present.

It is evident that within the limits employed here the effects of x-rays do not depend at all on the intensities at which a given dose is adminis-

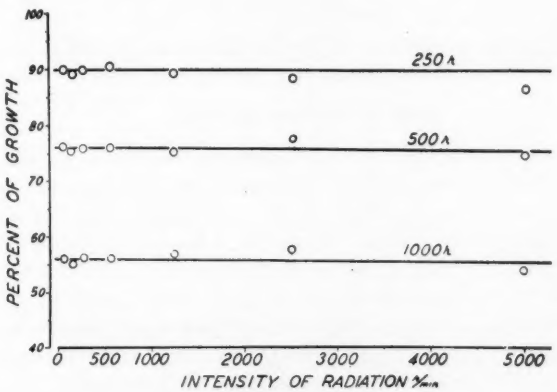

FIGURE 2

tered. It is possible that the density of ionization produced by x-rays even at 5000 r/min. is still much too small compared to density of ionization produced by alpha particles or by protons. It is also possible that the character of the action of the two types of radiation is different.

[1] G. Failla, *Jour. Appl. Phys.*, **12**, 279 (1941) Arthur A. Bless, *Proc. Nat. Acad. Sci.* **23**, 194 (1937).

[2] Florence E. Meier, *Smiths. Misc. Coll.*, **95**, 2 (1936).

[3] R. E. Zircle, *Am. Jour. Canc.*, **23**, 558 (1933).

[4] R. E. Zircle and P. C. Aebersold, *Proc. Nat. Acad. Sci.*, **22**, 134 (1936). John H. Lawrence and Robert Tenant, *Jour. Exp. Med.*, **66**, 667 (1937). R. E. Zircle and Isadore Lampe, *Am. Jour. of Roent. and Rad. Ther.*, **39**, 613 (1938). *A. Marshak Proc. Soc. Exp. Biol. and Med.*, **41**, 176 (1939).